REQUEST FOR RECONSIDERATION UNDER 37 C.F.R. §1.111

A. Status of the Claims

Claims 72, 73, 78, 79, 84, 86, 88-91 and 94-110 were indicated in the Action as pending in the case. It is thus believed by Applicants that the Examiner has renumbered claims 100-114 to 96-110 due to the omission of claim number 96-99 in the application as filed and in subsequent Preliminary Amendments. Claims 100-114 have thus been renumbered herein accordingly to 96-110. Claims 72, 73, 78, 79, 97 and 98 have been amended herein. The amendments correct several clerical errors in the claims and further clarify the claim language. A marked copy of the claim and specification amendments is included herewith as Appendix A. Support for the amendments to the claims can be found in the claims as filed. Claims 72, 73, 78, 79, 84, 86, 88-91 and 94-110 are now pending in the case and are presented for reconsideration.

B. Objections

The Action objects to the abstract as containing more than 150 words. In response, Applicants note that the abstract has been amended herein to include no more than 150 words. The amendment adds no new matter to the application. The rejection is now believed to be moot and removal of the objection is thus respectfully requested.

C. Rejections Under 35 U.S.C. §112, First Paragraph – Written Description

Claims 72-73, 78-79, 84, 86, 88-91, and 94-110 stand rejected under the first paragraph of 35 U.S.C. §112 as allegedly lacking an adequate written description of the claimed invention. In particular, the Action alleges that the specification does not describe preselected DNA sequences encoding an mRNA molecule which is substantially identical, or complementary to an

mRNA encoding a plant seed storage protein and related compositions. Applicants respectfully traverse.

It is first noted that the claims have been amended to clarify that the seed storage protein is a 19 kD or 22 kD α-zein plant seed storage protein. Further, Applicants do not generally claim 19 kD and 22 kD α-zein plant seed storage protein genes *per se*, as this class of genes was known at the time the application was filed, but rather transgenic plants expressing these proteins or methods comprising the use thereof are claimed. It is next noted that the structural features unique to a maize "19 kD and 22 kD α-zein plant seed storage protein" have been fully described in the specification. Accordingly, it can not be said that Applicants lack written description for the terms. In this regard, the Examiner's attention is directed to FIG. 1 of the application. There shown are functional domains that are conserved and shared among the zeins. Further attention is drawn to pages 1-3 of the application. There, the specification describes the family of know zeins, including 19 kD and 22 kD α-zeins. For example, at page 2, it is indicated, with a citation to Rubenstein (1982), that over 70 genes encoding zein protein have been isolated. Further on page 2, at lines 19-24, functional domains of 19 kD α-zeins are described. The structural characteristics of the 19 kD and 22 kD α-zein plant seed storage proteins have thus been described in full compliance with 35 U.S.C. §112, first paragraph and *Eli Lilly* is inapplicable to the instant situation.

The specification still further describes 19 kD and 22 kD α-zein seed storage proteins in the form of the nucleic acid sequence of the A20 and Z4 cDNAs, respectively. While these sequences are species of 19 kD and 22 kD α-zein protein genes, the species are representative of the genus as evidenced by Marks *et al.* (1985), which is cited at page 5 of the Action. Marks *et al.* demonstrates the common structural characteristics shared among 19 kD and 22 kD α-zeins.

For example, in the first sentence of the Abstract of Marks *et al.*, it is indicated that a comparison of the protein and DNA sequences of zein cDNA clones "reveals that they share extensive sequence homology and probably originated from a common ancestral gene." In the first paragraph of the Discussion section it is indicated that cDNA sequences among the 19 kD and 22 kD group of α-zein sequences are 75 to 95% and 92% homologous, respectively. Further, Marks *et al.* provides sequence information and comparisons among 19 kD and 22 kD α-zeins. The disclosure of Marks *et al.* thereby demonstrates the shared structural characteristics of the 19 kD and 22 kD α-zein seed storage proteins. Combined with Applicants' disclosure of the structural characteristics of 19 kD and 22 kD α-zein proteins, this is more than adequate to demonstrate compliance with the written description requirement.

In view of the foregoing, Applicants assert that the written description requirement has been fully satisfied. Removal of the rejection under 35 U.S.C. §112, first paragraph is thus respectfully requested.

D. Rejections Under 35 U.S.C. §112, First Paragraph - Enablement

Claims 72-73, 78-79, 84, 86, 88-91 and 94-110 stand rejected under the first paragraph of 35 U.S.C. §112 as allegedly not being enabled by the specification. In particular, the Action alleges that the specification does not teach one of skill how to increase the starch content or starch extractability or kernel hardness of seeds. It is stated that the specification only teaches how to make maize seeds with decreased amounts of the amino acid leucine and increased lysine by transforming *Zea mays* plants with SEQ ID NOs: 1 and 2 operably linked to a Z10 promoter. Applicants respectfully traverse.

The claims are fully enabled by the specification. While the Action notes that of four independent lines representing 8 samples in Table V of page 78, only three samples are said to exhibit a statistical increase in lysine compared to a control, this is irrelevant to enablement. What is relevant is that the Application teaches one of skill in the art to make and use the claimed invention without undue experimentation. An indicated success rate of 3/8 can not reasonably indicate undue experimentation, as it would be well within the capabilities of one of skill in the art to readily produce many lines expressing 19 kD and 22 kD α-zein plant seed storage proteins without undue experimentation using the methodology described in the specification. Should the Examiner wish, Applicants would gladly provide a declaration under 37 C.F.R. § 1.132 to this effect. Further, the fact that three of eight samples exhibited a statistical increase in lysine demonstrates the repeatability and enablement of the technique.

The Action cites Coleman *et al.* (1997) as teaching that the reduction of α-zein content "is concomitant with an inferior endosperm quality." However, it is noted that the claims are not directed to a subjectively "superior" endosperm and that what is "inferior" depends upon the use the plant is put to. What is considered inferior for a plant used to extract starch is not necessarily the same as for a plant put to other uses. Further, an "inferior endosperm" does not equate to an inability to increase starch content or extractability. On the contrary, Coleman *et al.* *demonstrates* the enablement of applicants claims. As indicated at page 7094, paragraph 2 of Coleman *et al.*, the endosperm of the high lysine *opaque2* and *floury2* mutants are said to be inferior because they are "soft, starchy endosperms." Indeed, this paragraph refers to the endosperm of the mutants as "starchy endosperm". This supports enablement by indicating that these mutants, which both involve aberrant expression of α-zeins, have both starchy and soft endosperm, which by virtue of these characteristics can be expected to exhibit increased

extractability. The fact that Coleman *et al.* also demonstrated successful expression of a 24 kDa α-zein gene to induce the mutant phenotype provides still further evidence of enablement of the instant claims by showing the broad applicability of the invention.

The other reference cited in the rejection, Marks *et al.* (1985), also supports the enablement of the invention. Marks *et al.* states in the abstract that:

> "A comparison of the DNA and protein sequences of a group of zein cDNA clones reveals that they share extensive sequence homology and probably originated from a common ancestral gene. A comparison of clones corresponding to Mr 22,000 polypeptides shows that they are 92% homologous, while five clones corresponding to Mr 19,000 zein vary in homology from 75 to 95%."

A strong structural relation among these zeins is thus indicated. As indicated above, this is also supported by the data presented in FIG. 1 of the specification. Further, mRNA differences in a transcriptional start site or a polyadenylation site do not necessarily indicate differences in coding sequences or in susceptibility to the methods of the present invention. No basis has been provided for the assertion in the Action that different isoforms have "divergent functions" and the high degree of homology and indicated common ancestor among zeins strongly contradicts the assertion. Additionally, there is no support in the Marks *et al.* reference for the contention that any of the mRNA isoforms described encode proteins other than zeins, the function of which is that of a seed storage protein. The conserved structure of the 19 kD and 22 kD α-zein plant seed storage proteins therefore demonstrates the broad applicability of the invention.

In view of the foregoing, Applicants submit that the claims are of a proper scope and are commensurate with the provided description. Removal of the rejection under 35 U.S.C. §112, first paragraph is thus respectfully requested.

E. Rejection of Claims Under 35 U.S.C. §101

The action has provisionally rejected claims 78, 79, 101 and 102 under 35 U.S.C. §101 as allegedly being directed to non-statutory subject matter. The rejection is made based on the possibility that, due to Mendelian inheritance of genes, a single gene introduced into a parent plant would not be transferred to a given progeny of that plant. With respect to claims 78 and 79, Applicants note that the claims has been amended to specify that the progeny inherit the preselected DNA. With respect to claims 101 and 102, Applicants note that the claims are not directed to seed and instead are method claims directed to use of transgenic plants. The rejection is thus not understood and not believed applicable to these claims.

In view of the foregoing, removal of the rejection is respectfully requested.

F. Rejection of Claims Under 35 U.S.C. §112, Second Paragraph

The Action rejects claims 88-89, 90, 91 and 102-107 under 35 U.S.C. §112, second paragraph for allegedly being indefinite for failing to particularly point out the subject matter which Applicant regards as the invention. In particular, the Action rejects the claims as being indefinite for the recitation of "substantially complementary to all or a portion" and "substantially identical to all or a portion". In particular, it is stated that the recited phrases are vague and unclear and don't specify what portion or percent of the sequence applicants are referring to.

In response, it is first noted that the claims have been clarified to indicate that the RNA is substantially identical, or complementary to, an mRNA encoding a 19kD or a 22kD α-zein plant seed storage protein. It is further noted that the terms "substantially identical" and "substantially complementary" are defined in the specification at page 12, lines 11-24. The use of the terms in

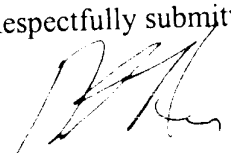
the claims is thus not indefinite. Still further, the claims define the terms by indicating that expression of the seed storage protein RNA decreases the amount of seed storage protein. Thus it is clear that substantially identical to or complementary to all or a portion refers to those sequences that are complementary such as to hybridize with the seed storage protein mRNA *in vivo* to cause antisense suppression. Such a sequence could not represent a single homologous base pair, as it is well known that in order to form the type of stable complex required for antisense suppression, longer stretches of complementary sequences are required. The cited terms are thus fully definite. The second paragraph of 35 U.S.C. §112 merely requires that it be clear to those skilled in the art what Applicant intends to claim. What is dispositive is whether one of ordinary skill in the art would understand what is claimed when the claims are read in light of the specification. Given the definition in the specification and claim language, the referenced terms fully meet this requirement.

In light of the foregoing, Applicant hereby respectfully requests that the rejection of claims 88-89, 90, 91 and 102-107 under 35 U.S.C. §112, second paragraph, be withdrawn.

G. Conclusion

In light of the foregoing, applicants submit that all claims are in condition for allowance, and an early indication to that effect is earnestly solicited. The examiner is invited to contact the undersigned (512)536-3085 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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Date: June 13, 2002

APPENDIX A: VERSION OF AMENDMENTS MARKED TO SHOW CHANGES

In the Specification:

At page 122, line 2, please replace the Abstract with the following:

--The invention provides [genetically engineered,] preselected DNA sequences and methods of using them to alter the nutritional content of plant seed. Methods of the invention are directed to increasing the weight percent of [at least one] an amino acid essential to the diet of animals, or increasing the starch content, of a plant. One [such] method involves stably transforming a cell of a plant with [an] a preselected DNA sequence encoding an RNA molecule substantially identical or complementary to a messenger RNA [(mRNA)] encoding a plant seed storage [protein, preferably a seed storage protein which is deficient in at least one amino acid essential to the diet of animals.] protein. An alternative method employs stably transforming cells with at least two preselected DNA sequences, one of which encodes an RNA molecule substantially identical or complementary to a messenger RNA (mRNA) encoding a plant seed storage protein, and the other preselected DNA molecule which encodes a preselected polypeptide. The transformed cells are used to generate fertile transgenic plants and [seeds. Transgenic seeds] seeds, which are characterized by expression of the preselected DNA [sequence which results in a substantial inhibition of production of a seed storage protein deficient in at least one amino acid essential to the diet of animals and/or an increase in the weight percent of an amino acid essential to the diet of animals.] sequence.--

In the Claims:

Please cancel claim 94 without prejudice or disclaimer.

Please amend claims 72, 73, 78, 79, 97 and 98 as indicated below:

72. (Twice Amended) A fertile transgenic *Zea mays* plant having an increased starch content, the genome of which is stably augmented by a preselected DNA sequence encoding an RNA molecule which is substantially identical, or complementary, to an mRNA encoding a 19kD or a 22kD α-zein plant seed storage protein, wherein the preselected DNA sequence is expressed in the cells of the transgenic plant in an amount sufficient to

decrease the amount of said seed storage protein and increase starch content in the cells of a plant which only differ from the cells of said transgenic plant in that said preselected DNA sequence is absent, and wherein said preselected DNA sequence is transmitted through a complete normal sexual cycle of the transgenic plant to the next generation.

73. (Twice Amended) A fertile transgenic *Zea mays* plant, the seeds of which have an increased starch extractability, the genome of said plant which is stably augmented by a preselected DNA sequence encoding an RNA molecule which is substantially identical, or complementary, to an mRNA encoding a 19kD or a 22kD α-zein plant seed storage protein, wherein the preselected DNA sequence is expressed in the seeds of the transgenic plant in an amount sufficient to decrease the amount of said seed storage protein and increase the starch extractability of the seed relative to the amount of said seed storage protein and starch extractability in the seeds of a plant which only differ from the seeds of said transgenic plant in that said preselected DNA sequence is absent, and wherein said preselected DNA sequence is transmitted through a complete normal sexual cycle of the transgenic plant to the next generation.

78. (Twice Amended) A seed derived from the plant of claim 72 or 73, wherein the seed comprises said preselected DNA sequence.

79. (Twice Amended) A p[P]rogeny plant derived from the seed of claim 78, wherein the plant comprises said preselected DNA sequence.

97. (Amended) A method of producing a *Zea mays* seed with an increased starch content, comprising:

(a) growing a transgenic *Zea mays* plant, the genome of which is augmented with a preselected DNA sequence encoding an RNA molecule which is substantially identical, or complementary to an mRNA encoding a 19kD or a 22kD α-zein seed storage protein, wherein the preselected DNA sequence is expressed in the cells of the *Zea mays* plant in an amount sufficient to decrease the amount of seed storage protein; and

(b) selecting a seed from the transgenic *Zea mays* plant, wherein the seed has an increased amount of starch relative to the amount of starch in a seed selected from a plant which does not comprise said preselected DNA sequence.

98. (Amended) A method of obtaining starch from a *Zea mays* seed, comprising:

(a) growing a transgenic *Zea mays* plant, the genome of which is augmented with a preselected DNA sequence encoding an RNA molecule which is substantially identical, or complementary, to an mRNA encoding a 19kD or a 22kD α-zein seed storage protein, wherein the preselected DNA sequence is expressed in the cells of the *Zea mays* plant in an amount sufficient to decrease the amount of seed storage protein;

(b) obtaining seed from said plaint; and

(c) extracting starch from the seed.